Spinal Cord Diffusion Imaging

Imaging Challenges and Prognostic Value

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Part I

INTRODUCTION

1

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Motivation

The spinal cord is a vital part of the human central nervous system (CNS), relaying information to and from the brain and controlling the motor function in the rest of the body. Damage to the spinal cord tissue will compromise signal transmission and can cause severe neurological symptoms, often resulting in a loss of mobility or feeling. Spinal cord injury (SCI) is often caused by trauma, i.e., a mechanical injury of the cord tissue during an accident, fall, etc. However, SCI can also have non-traumatic causes, such as tumours, infectious diseases or degenerative pathologies of the CNS like Multiple Sclerosis (MS).

The introduction of Magnetic Resonance Imaging (MRI) to the clinical practise has vastly improved the diagnosis and treatment monitoring of SCI as it offers a non-invasive way to assess anatomical changes in the spinal cord after injury. While routine MRI scans are aiding the detection of macroscopic changes in the cord, they have a limited prognostic value because of their qualitative nature and because of their lack of specificity in terms of underlying microstructure changes.

The sensitivity of Diffusion Weighted Imaging (DWI) to the diffusion of water molecules in the tissue in vivo has been exploited for more than 20 years to characterise the white matter tissue structure of the brain. Thanks to technological advances such as multi-channel coils for parallel imaging methods and 3T scanners, the past couple of years have made their application of DWI in the spinal cord (SC) more feasible. As a result, diffusion imaging techniques are emerging as useful clinical for methods for visualization and quantification of spinal cord damage. Despite encouraging initial results, much work need still to be done to bring DWI in the cord to clinical practise. Specifically there is the need for in-vivo imaging biomarkers for human SC examinations, which are sensitive to underlying tissue changes and which are capable of quantifying structural and functional pathologies.

1.1 Problem statement

Despite some development work on DWI for SC, the following problems are mainly unresolved

1. Current state-of-the-art DWI analysis methods, such as Diffusion Tensor Imaging (DTI), are unspecific to individual microstructural changes and therefore only have limited value in the evaluation of treatment and recovery in spinal cord pathology. Research on more advanced DWI techniques is usually focussed on the only the brain in mind and is often not directly applicable to the SC in the same manner.

2. DWI acquisition itself is well established in the brain, but much less so in the SC. The SC is a more challenging structure to study because of several problems: the breathing motion, the artefacts arising from the surrounding bones, the pulsation of the cerebro-spinal fluid (CSF) and last but not least its limited size that requires high resolution.

The key motivation of this work is to overcome the challenges above by optimising the whole process from the acquisition design to the analysis methods, based on known SC tissue properties and to develop imaging biomarkers can provide insight in underlying mechanisms of tissue damage and functional recovery.

1.2 Aims

1. Investigate existing DWI methods and identify suitable metrics for SC characterisation

2. Optimise existing acquisition protocols and analysis methods to improve sensitivity to SC pathologies

3. Design new DWI imaging protocols and white matter models and derive new imaging biomarkers specifically for a better quantification of SC microstructure properties

1.3 Summary of contributions

The work presented in this dissertation is divided in three parts, comprising 8 different experiments in total. Each part contributes towards the aims described above as follows:

Part **??** shows two studies that use the well established DTI method.

Chapter **??** devises a novel imaging protocol to visualise and quantify the presence of collateral sprouting fibres at different levels of the SC. This experiment contributes towards project aim 1 and 2 as we investigate two different DWI metrics from existing literature and focus on the optimisation of the acquisition protocol.

In Chapter **??** we develop a novel post-processing method that corrects average DTI metrics for partial volume effects. This experiment contributes towards project aim 2, as we aim to improve reliability and reduce inter-subject variability for DTI acquisitions and measurements that are widely used in clinical studies.

Part **??** presents two studies which implement the less commonly used q-space imaging (QSI) method in the cord. The aim is to test whether is is possible to distinguish different parts of the healthy human cord by their QSI parameters. The two experiments contributes towards project aim 1 as they test the use of QSI metrics for the investigation of SC microstructure. The experiments also contribute to project aim 3 as they look for the first time into QSI parallel to the major fibre direction as an additional imaging marker.

Chapter **??** presents data that was analysed retroactively on already acquired QSI-data. This dataset data revealed interesting results, but was put in question by technical limitations of the acquisition and analysis method.

Chapter **??** presents our effort to reproduce the results of Chapter **??** on our newly installed 3T scanner, which allowed us more control over the scan parameters than before.

Part **??** shows our work towards project aim 3 by developing DWI protocols that allow direct estimation of axon diameter and density of SC white matter tissue. Our $\mathcal{SF}$ method is an extension of the "ActiveImaging" framework by Alexander et al. (2010), which we modify to be able to exploit the characteristic a-priori know single major fibre orientation in structures like the SC. To aid the initial development we use in some experiments the corpus callosum as a model system of highly coherent white matter structures, similar to the SC organisation.

Chapter **??** presents a first implementation of the $\mathcal{SF}$ method. We use synthetic dataset from computer simulations to evaluate

our method and compare with Alexander's original method and further show results of a first real-world implementation of our method applied to ex-vivo monkey spinal cord.

Chapter **??** introduces several improvements to our first $\mathcal{SF}$ implementation and presents a first implementation of the $\mathcal{SF}$ method in-vivo on a standard clinical scanner on two healthy volunteers.

Chapter **??** brings together our efforts in improving image quality and DWI acquisition protocols. We here devise a novel imaging and analysis pipeline for $\mathcal{SF}$-ActiveImaging and assess its scan/rescan reproducibility in the human corpus-callosum. Furthermore, we also present a first application of $\mathcal{SF}$ to the healthy in-vivo human cord in one subject.

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